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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,240	10/21/2005	Jan Henrik Ardenkjaer-Larsen	PS0269	8192

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EXAMINER	
SCHLIENTZ, LEAH H	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
08/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,240	ARDENKJAER-LARSEN ET AL.	
	Examiner	Art Unit	
	Leah Schlientz	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/23/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *12-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 1/23/08 is acknowledged.

Status of Claims

Claims 1 – 16 are pending, of which claims 12 – 16 are withdrawn from consideration at this time as being drawn to a non-elected invention. Claims 1 – 11 are readable upon the elected invention and are examined herein on the merits for patentability.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 – 11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a method for producing an MR contrast agent, the method comprising the steps of: -obtaining a

solution in a solvent of a hydrogenatable, unsaturated substrate compound and a catalyst for the hydrogenation of a substrate compound, wherein the substrate compound comprises imaging nuclei. However, the specification does not provide description of the claimed hydrogenatable, unsaturated substrate compound required to make and use the contrast agent as broadly claimed. There is no description provided regarding which types of specific chemical moieties are used to represent the substrate that would render such a compound to be useful as a contrast agent. There is very little predictability in the art concerning any undefined species which may represent a substrate compound and furthermore, one of ordinary skill in the art would not know which chemical moiety would represent a substrate out of an almost unlimited number of chemical species which may be possible. The specification does not provide any guidance to the specific identity or physical / chemical structure of the variables which represent a substrate, and because the structures and physical identities of these elements are undefined, it is unclear how Applicant envisaged suitable elements to satisfy the functional requirements of the substrate. It is noted that the specification refers to suitable substrate materials as those found in WO 99/24080, however, the incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the

material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 – 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to a method for producing MR contrast agent comprising the steps of -*obtaining* (100) a solution in a solvent of a hydrogenatable, unsaturated substrate compound...; -*hydrogenating* (105) the substrate...; and -*exposing* (110:705) the contrast agent to a magnetic field cycling profile adapted for enhancing the contrasting effects of the contrast agent. Dependent claims 2 – 11 further include various –*placing* (700) and -*removing* (710), -*finding* (400) etc. steps. The claims also refer to various magnetic field fluctuations: decrease (705.01) or increase (705.02), and various apparatus parts: magnetic field screen (247) or magnetic treatment chamber (246). The numbers included in parenthesis appear to refer to figures in the specification (see Figures 1 – 7). However, where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." Ex parte Fressola, 27 USPQ2d

1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations omitted). Reference characters corresponding to elements recited in the detailed description and the drawings may be used in conjunction with the recitation of the same element or group of elements in the claims. See MPEP § 608.01(m). See also 2173.05(s). In the instant case, the claims appear to be adequately described using text and the reference to the figures via various step numbers is unnecessary. It is respectfully suggested that the claims should be amended to remove the step numbers and apparatus numbers in parentheses.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 – 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Axelsson *et al.* (WO 00/071166, whereby US 6,872,380 is relied upon as equivalent).

Axelsson discloses a process for the preparation of an MR contrast agent comprising: (i) obtaining a solution in a solvent of a hydrogenatable, unsaturated substrate compound and a catalyst; (ii) introducing said solution in droplet form to a chamber containing hydrogen gas enriched in para-hydrogen and/or orthodeuterium, whereby to hydrogenate said substrate to form a hydrogenated imaging agent; (iii) optionally subjecting said hydrogenated imaging agent to a magnetic field strength

below earth's ambient filed strength (column 2, lines 39+). Preferably, the low field treatment may be effected by passage through a magnetically shielded area with a special magnetic field profile. The sample leaves earth's magnetic field (i.e. an initial decrease in magnetic field, as instantly claimed) and enters an area with a field lower than 0.1 μT (i.e. 100 μT, as instantly claimed) in just a few ms. The sample is then gradually returned to the earth's magnetic field (i.e. at least one increase of the magnetic field). This effects an efficient transfer of polarization from protons to the hetero-nucleus (column 3, lines 20 - 33). With regard to instant claims 4 – 9, the cycling of the external magnetic field from "earth-field" to less than 1 μT, preferably about 0.1 μT, and then gradually back again enables polarization to be transferred from protons in the freshly hydrogenated contrast agent to nucleus within the same molecule, preferably ^{13}C. The timing of the process is critical. The sample should leave the earth-field suddenly (i.e. decrease in magnetic field), which means on the order of 1 ms. The sample should then gradually return to earth field (i.e. increase in field), meaning on the order of 10-10000 ms, preferably 100-1000 ms. It is noted that Axelsson does not specifically recite the magnetization profile such that non-adiabatic remagnetization occurs, however, it is interpreted in the absence of evidence to the contrary that such a process would inherently occur in the method disclosed by Axelsson. This interpretation is supported by Applicant's specification, which describes the correlation of adiabatic/non-adiabatic processes as depending on the rate of magnetization. Since Axelsson meets the requirements of the rates of decrease and increase of magnetic fields as defined in the dependent claims, it is interpreted that the method of Axelsson

also inherently meets the limitation of non-adiabatic remagnetization. With regard to instant claim 10, the claim does not provide any active steps over those which are performed by Axelsson. The claim is merely descriptive regarding the magnetic field cycling parameters (e.g. the method according to claim 1 wherein the cycling field profile *is described with* a set of field cycling parameters, etc. having various functional language). With regard to instant claim 11, it is noted that the step of demagnetizing under a magnetic field screen of the magnetic treatment chamber utilizing a demagnetization circuit comprising demagnetization coils is optional, however, Axelsson discloses such a step (see column 4, lines 1 - 20).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 – 11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 3 - 6 of copending Application No. US 10/526,238. Although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims are drawn to a method of producing an MR contrast agent comprising the steps of obtaining a solution of a hydrogenatable, unsaturated compound, hydrogenating with parahydrogen enriched hydrogen gas, and exposing the contrast agent to a magnetic field. With regard to the exposing step, the instant application requires an initial decrease in magnetic field followed by at least one increase of magnetic field and that of the '238 application requires placing the contrast agent in a magnetic field on the order of earth's magnetic field and subjecting the contrast agent to subsequent magnetic field having different strength, orientation or duration to that of the earth's field and returning to earth's field. Accordingly, the claims are overlapping in scope and are obvious variants of one another. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS